Alternations of Transient Outward K⁺ Current (Ito) in Type 2 Diabetic Ventricular Cardiomyocytes

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**Background:** Although cardiac ion channel remodeling has been reported in type 1 diabetes mellitus (T1DM), modification of the channels by type 2 DM (T2DM) is poorly understood. Here we characterized ion channel properties in cardiomyocytes of OLETF, a rat model of obese T2DM.

**Methods and Results:** We isolated myocytes from subepicardial (EPI) and subendocardial (END) regions of the left ventricle for whole-cell patch clamp experiments. Action potential duration at 50% repolarization (APD₅₀) at 1 Hz was significantly longer in OLETF than in non-diabetic control (LETO) (EPI: 8.89±1.04 vs. 5.20±0.75 ms, END: 22.01±3.64 vs. 9.89±1.74 ms). In both EPI and END, L-type Ca²⁺ current and inward rectifier K⁺ current were similar between OLETF and LETO. In EPI, transient outward K⁺ current (Ito) density at 0.1 Hz was similar. However, the fast recovering component from inactivation of Ito was significantly decreased in OLETF. In END, Ito density at 0.1 Hz was significantly reduced in OLETF (8.77±0.78 vs. 14.50±1.31 pA/pF at +60 mV), in addition to slower recovery of Ito. Membrane capacitances were similar in all groups. **Conclusions:** T2DM slowed Ito recovery form inactivation and decreased END-Ito density without cardiomyocyte hypertrophy. This regional difference in the effect on Ito has not been reported for T1DM and appears characteristic to T2DM.

**Keywords:** diabetic cardiomyopathy, transient outward potassium current, action potential